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Original Article

Oral Dexamethasone to Control Wheezing in Children at an Outpatient Clinic

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Abstract

Asthma, a chronic childhood disease, has resulted in increased emergency department (ED) visits with high costs. Many asthma ED visits are nonemergent and could be treated in outpatient clinics. Literature has concluded that a 2-day course of oral dexamethasone has comparable outcomes to a 5-day course of prednisone in the ED and hospital setting. A retrospective chart review was performed on children requiring in-house treatment with a corticosteroid (dexamethasone n = 23, prednisone n = 40) for acute asthma exacerbations at an ambulatory medical home. The rates of hospital admissions, ED visits, and symptom follow-up were similar between the 2 groups ($P > .05$). The cost for a course of dexamethasone was US$1.28 versus US$16.20 for prednisolone. The average cost for an asthma exacerbation office visit was US$79.89 compared with US$3113.28 for an ED visit. A 2-day course of oral dexamethasone appears to be a promising clinical and cost-effective treatment for acute asthma exacerbations at the primary care level.

Keywords

asthma, wheezing, pediatrics, corticosteroid, dexamethasone, medical home, primary care, cost

Introduction

Asthma currently affects over 6 million children and is the most common chronic childhood disease.[1,2] Recent initiatives, in accordance with the National Heart, Lung, and Blood Institute guidelines, have aimed to control asthma symptoms by providing education to children and families through training and outreach programs.[3-8] Despite these recommendations, emergency department (ED) visits for asthma-related symptoms remain high, with asthmatic children more likely to use the ED as a primary health care facility.[1] Pediatric ED visits for the treatment of asthma surpassed 629 000 visits in 2010 for Medicaid/CHIP (Children's Health Insurance Program) enrollees,[9] with a reported total cost of US$272 million.[9]

Due to the high burden of disease, EDs have instituted protocols for the safe and effective management of pediatric asthma visits,[10,11] with a decline in hospital admissions seen between the years 2000 and 2010.[12] Evidence-based guidelines established by the National Institute of Health recommend the use of systemic corticosteroids along with β-agonist therapy in the treatment of acute asthma exacerbations.[3,13-15] Corticosteroids decrease inflammation and potentiate the effects of bronchodilators, preventing symptom recurrence and decreasing hospital admission rates.[2,16-19]

Recent studies have investigated the use of different treatment options involving systemic corticosteroids in the ED and hospital settings for acute asthma exacerbations. Traditional therapy has included the short-acting corticosteroid prednisone or its derivative prednisolone.[19-21] With a half-life of 12 to 36 hours, these medications are typically prescribed as an oral tablet or liquid formula for 5 days. A high rate of treatment nonadherence has resulted from its poor taste, high emesis rates, and a longer treatment duration.[2,14,22] Recent investigations have looked to the use of a long-acting corticosteroid, dexamethasone, with a half-life of 36 to 72 hours requiring only a 2-day treatment

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course. This potent medication, with better palatability and a shorter duration of treatment, may have improved compliance rates.[14,21-24]

Literature suggests that 2 days of oral dexamethasone treatment for acute asthma exacerbations in the ED and hospital setting is just as effective in symptomatic treatment as a 5-day course of prednisone.[2,14,18,21,25-28] These studies have not been replicated in the ambulatory setting. A study by Bhogal et al showed that early administration of systemic corticosteroids reduced the odds of admission and length of treatment.[29] By providing effective treatment in primary care centers, the number of ED visits can be reduced. The goal of this study is to compare the use of oral dexamethasone versus prednisone in the treatment of acute asthma symptoms in the primary care setting. Primary endpoints include rates of hospital admissions, ED visits, and symptom recurrence. Secondary endpoints investigated differences in medication costs and costs of office versus ED visits.

Methods

After appropriate approval by the Baylor College of Medicine Institutional Review Board (H-37654), a retrospective chart review was conducted on all patients, who presented to The Center for Children and Women—Greenspoint (The Center) Pediatric Department in Houston, Texas. As a retrospective study, informed consent could not be obtained from patients included in this study. The Center, a branch of the Texas Children's Health Plan (TCHP), is a patient and family-centered practice offering primary care services including pediatrics, obstetrics and gynecology, behavioral health, optometry, dentistry, nutrition, speech, imaging, laboratory, and pharmacy services. The mission of the Center is to offer comprehensive, effective, primary care services for the Medicaid and CHIP population.[30] The electronic medical record (EMR) system was surveyed to identify patients ⩽18 years of age seen at the Center's Pediatric Department between August 2013 and July 2015, with a primary visit diagnosis of "wheezing" (ICD9 786.07), "asthma unspecified type with exacerbation" (ICD9 493.92), "asthma with status asthmaticus" (ICD9 493.91), or "cough variant asthma" (ICD9 493.82) based on documented *International Classification of Diseases, Ninth Revision, Clinical Modification codes*. All patients included in the study received an oral corticosteroid dose in clinic, with future doses prescribed and dispensed from the Center's pharmacy. For the care of acute asthma exacerbations, providers generally followed the National Asthma Education and Prevention Program (NAEPP) guidelines for the diagnosis and management of asthma,[3,13] which recommends an inhaled β-agonist, and based on symptom severity, also oral corticosteroids and possibly inhaled ipratropium. In the winter of 2014, the Center's providers were educated on the costs of prednisolone and dexamethasone and provided with information about the successful administration of dexamethasone in the emergency setting. Providers were able to prescribe either medication as they felt best for their patients. Only patients ⩾3 years of age were included in this study, to increase the likelihood of asthma as an established diagnosis rather than other causes of wheezing such as bronchiolitis. Children were excluded from the study if they received steroid treatment from an outside health facility within 1 week of presentation to the Center.

Demographic information was collected from the EMR including patient gender, age, race, as well as the Clinical Respiratory Score (CRS) at presentation. The full version of the CRS is shown in Table 1, incorporating clinical assessments to identify illness severity and recommend a treatment algorithm. Documentation of which oral corticosteroid was prescribed was also recorded as well as if patients were previously on an inhaled corticosteroid.

The Center has a standardized, evidence-based protocol in place for the rapid treatment initiation for acute asthma exacerbations. The protocol is initiated for patients presenting with wheezing, or increased work of breathing, and asthma. Asthma, defined by the protocol, is a patient ⩾2 years of age, with a CRS of ⩾3 and <8, and a history of asthma, or ⩾3 wheezing episodes treated with a β-agonist. The protocol is not initiated if the CRS is ⩾8, if systemic corticosteroids were administered within the proceeding 7 days, if the patient has a history of a chronic systemic disease (cystic fibrosis, transplant, cancer, etc), if the patient is allergic to corticosteroids, or if the patient has active emesis.

If the protocol is initiated, inhaled β-agonist treatment is begun, the patient is seen by a provider, and an oral corticosteroid is administered, either prednisolone or dexamethasone. The patient is also placed on continuous pulse oximetry monitoring and administered supplemental oxygen if oxygen saturations fall below 94%. If dexamethasone is used, a single dose of a dissolvable oral tablet using a weight-based formula (Table 2) is administered at the Center. A single dose of weight-based prednisolone (1-2 mg/kg, maximum 60 mg/day), as either an oral tablet or liquid solution, is used for patients receiving this corticosteroid. Patients are monitored for clinical response to the treatment protocol and are referred to the ED if symptoms fail to improve or their clinical condition deteriorates. If patients are deemed clinically stable to be discharged home,

Table 1. Standard Clinical Respiratory Score (CRS).

Assess	Score 0	Score 1	Score 2
Respiratory rate (breaths per minute)	<2 months: <50 2-12 months: <40 1-5 years: <30 >5 years: <20	<2 months: 50-60 2-12 months: 40-50 1-5 years: 30-40 >5 years: 20-30	<2 months: >60 2-12 months: >50 1-5 years: >40 >5 years: >30
Auscultation	Good air movement, scattered expiratory wheezing, loose rales/crackles	Depressed air movement, inspiratory and expiratory wheezes or rales/crackles	Diminished or absent breath sounds, severe wheezing, or rales/crackles, or marked prolonged expiration
Use of accessory muscles	Mild to no use of accessory muscles, mild to no retractions, no nasal flaring on inspiration	Moderate intercostal retractions, mild to moderate use of accessory muscles, nasal flaring	Severe intercostal and substernal retractions, nasal flaring
Mental status	Normal to mildly irritable	Irritable, agitated, restless	Lethargic
Room air SpO_2	>95%	90% to 95%	<90%
Color	Normal	Pale to normal	Cyanotic, dusky

Abbreviation: SpO_2, saturation of peripheral oxygen.

Table 2. Weight-Base Dexamethasone Dosing.

Current Standardized Dosing			Tablet
Weight (kg)	Dose (mg)	mg/kg	1 mg and 4 mg
5-7.5 kg	4.5 mg	0.6-0.9 mg/kg	4 mg
>7.5-10 kg	6 mg	0.6-0.8 mg/kg	4 mg + 2 × 1 mg
>10-15 kg	9 mg	0.6-0.9 mg/kg	2 × 4 mg + 1 mg
>15-20 kg	12 mg	0.6-0.8 mg/kg	3 × 4 mg
>20 kg	16 mg	<0.8 mg/kg	4 × 4 mg

additional doses of the oral corticosteroid are prescribed and dispensed from the Center's pharmacy. One additional dose is prescribed for those receiving dexamethasone, to complete a 2-day course, and 4 additional days of treatment are prescribed to those receiving prednisolone, to complete a 5-day course. Prior to discharge home from the clinic, it is standard practice for practitioners to educate families on the importance of medication compliance and the use of inhaled bronchodilators according to an Asthma Action Plan, and a follow-up appointment is scheduled.

Primary outcomes of the study investigated rates of ED visits, hospital admissions, and return clinic visits within 1 week for recurrent or persistent symptoms, as documented in the EMR. TCHP insurance claims were also reviewed to obtain information on any additional health facility visits outside of the Texas Children's Network. The cumulative hospital, ED, and return to clinic visits were compared between the group of patients receiving oral dexamethasone and the group receiving oral prednisolone. The time until discharge from the clinic was also compared between the 2 groups. If there was no time of discharge recorded, the time when patient instructions were printed was used as the discharge time.

Additional outcomes assessed included direct treatment costs. Using the 50th percentile ideal body weight for a 7-year-old (average age of study patients) male of 23 kg,[31] the weight-based costs for a prescription of oral dexamethasone and oral prednisolone from the Center's pharmacy were obtained and compared. Insurance claims of the patients in our study were investigated to identify the average cost for an outpatient asthma exacerbation visit at the Center. To calculate the average cost of an ED asthma exacerbation visit, insurance claims from the study period were investigated for any pediatric patient 3 to 18 years of age from the Center seen at an ED with an ICD code for "asthma exacerbation." Claims with an ICD code "status asthmaticus" were not included as those cannot be effectively managed in the outpatient setting.

Statistical analysis was performed to test for significance. Pearson's χ^2 and Fisher's exact tests were used to test statistical differences of categorical data. A 2-sample *t* test with equal variances was used to compare sample means. A statistical significance was set at a *P* value less than .05 corresponding to a confidence level of 95%. All statistical analyses were done using STATA 14.0 (StataCorp LLC, College Station, TX).

Results

A total of 63 patient encounters met inclusion criteria for the study. The NAEPP guidelines for the treatment of acute asthma exacerbations was initiated for all patients, with an oral corticosteroid administered during their clinic visit. Sixty-three percent of patients were given oral prednisolone (n = 40), and 37% of patients received oral dexamethasone (n = 23). Sixty-nine percent of patients were of Hispanic descent. The mean patient age was 6.9 years (range = 3-16 years; SD 3). The majority

Table 3. Patient Demographics.

	Prednisone Group, N = 40	Dexamethasone Group, N = 23	*P*
Gender			1
Male	31	18	
Female	9	5	
Average age (years)	6.4	7.8	.06
Race			.3
Hispanic	24	17	
Non-Hispanic	16	6	
Patients' prior use of ICS			.8
History of ICS	15	7	
No ICS	25	16	
CRS at presentation			.8
Initial CRS ⩽2	19	13	
Initial CRS 3-4	15	8	
Initial CRS ⩾5	6	2	

Abbreviations: ICS, inhaled corticosteroid; CRS, Clinical Respiratory Score.

of patients were not previously on an inhaled corticosteroid, with only 38% of patients on this maintenance therapy prior to presentation.

Table 3 portrays patient demographics between the prednisolone and dexamethasone groups. No statistical difference was seen for gender, age, race, CRS at presentation, or patients' prior use of inhaled corticosteroids between the 2 groups ($P > .05$). Of the 40 patients who received prednisolone, 5 patients were referred to the ED and eventually discharged home, 3 patients were admitted to the hospital, and 2 patients returned to the Center within 1 week due to persistent symptoms. In the group that received oral dexamethasone, 1 patient was admitted and 1 patient was later seen in the ED for diagnosis of influenza and asthma. The remaining patients in both cohorts had no EMR documentation or insurance claims to suggest further escalation of care or follow-up needed. For 16% of patients, insurance claims from outside facilities were not traceable. Using the Fisher's exact test, no significant difference was found for the cumulative hospitalizations, ED visits, or follow-up clinic visits for recurrent symptoms for either group ($P > .05$; Figure 1). Looking at the average time until discharge from the Center, no significant difference ($P > .05$) was seen between those receiving prednisone ($t = 122$ minutes) and those receiving dexamethasone ($t = 118$ minutes; Figure 2).

Using a 7-year-old 23 kg male as reference, the prescription cost for a 2-day course of oral dexamethasone was US$1.28, and the cost for a 5-day course of prednisolone was US$16.20. TCHP insurance claim information was also used to identify costs for asthma exacerbation visits at the Center and the ED. For the patients included in our study, the average cost for an asthma exacerbation office visit at the Center was US$79.89. During the study period, there were a total of 55 claims for asthma exacerbations at EDs among all pediatric patients at the Center, which averaged US$3113.28 per ED visit.

Discussion

This study shows promising results in providing effective treatment in the primary care setting for acute pediatric asthma exacerbations. Comparing the use of a 2-day course of oral dexamethasone to a 5-day course of oral prednisolone, no statistically significant difference was seen in the rate of ED visits, hospital admissions, and return visits to clinic for persistent or recurrent symptoms ($P > .05$). The use of either medication in our primary care clinic is equally effective suggesting a safe alternative to the 5-day prednisolone regimen.

To our knowledge, this is the first study comparing the use of oral dexamethasone to oral prednisone/prednisolone in an ambulatory setting. The literature has demonstrated similar outcomes between the 2 medications when used in the ED setting. A study published in 2001 by Qureshi et al was one of the first studies to compare these medications. The prospective randomized trial revealed similar relapse rates measured as return medical visits within 10 days, concluding similar efficacies.[25] Paniagua et al later reported no difference in recurrent symptoms, quality of life within 7 days, admission rates, and additional ED visits.[2] A systematic review, performed by Abaya et al again revealed a similar efficacy with regard to return ED visits.[18]

Our study focused only on oral medication administration, as this is the routine route in the primary care setting. Consensus in the literature also agrees that the oral administration of a 2-day course of dexamethasone and a 5-day course of prednisone provide similar results when prescribed in the ED for asthma exacerbations.[18,25] Studies further sought to investigate different routes and doses of administration to increase generalizability. A systematic review and meta-analysis conducted by Keeney et al looked at the oral or intramuscular administration of dexamethasone compared with oral prednisone in the ED. Still, no differences were seen in relapse rates.[26]

Meyer et al conducted a meta-analysis to compare these medications in the inpatient setting. Evaluating the

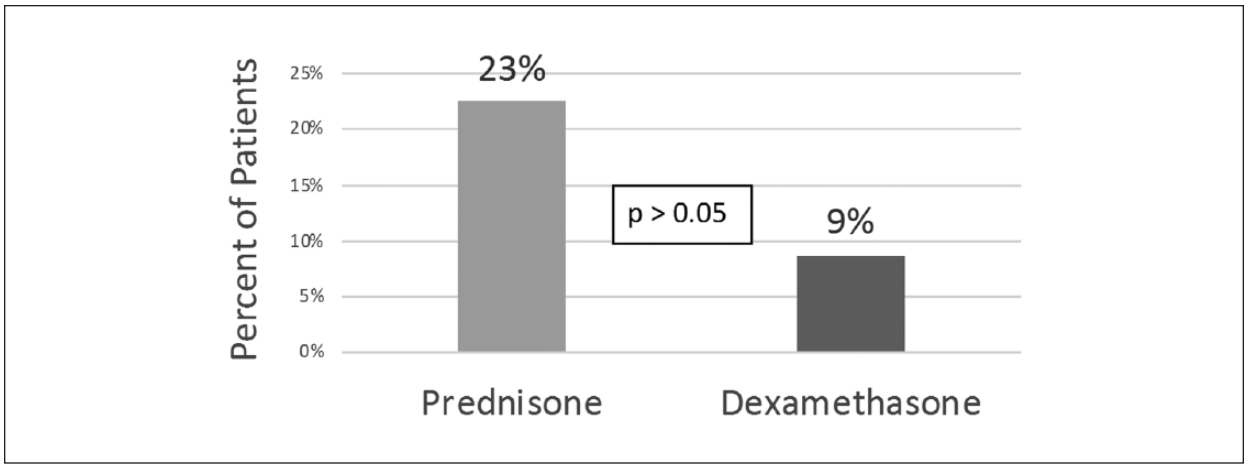

Figure 1. Comparison of cumulative hospitalizations, emergency department (ED) visits, and return clinic visits between prednisone and dexamethasone.

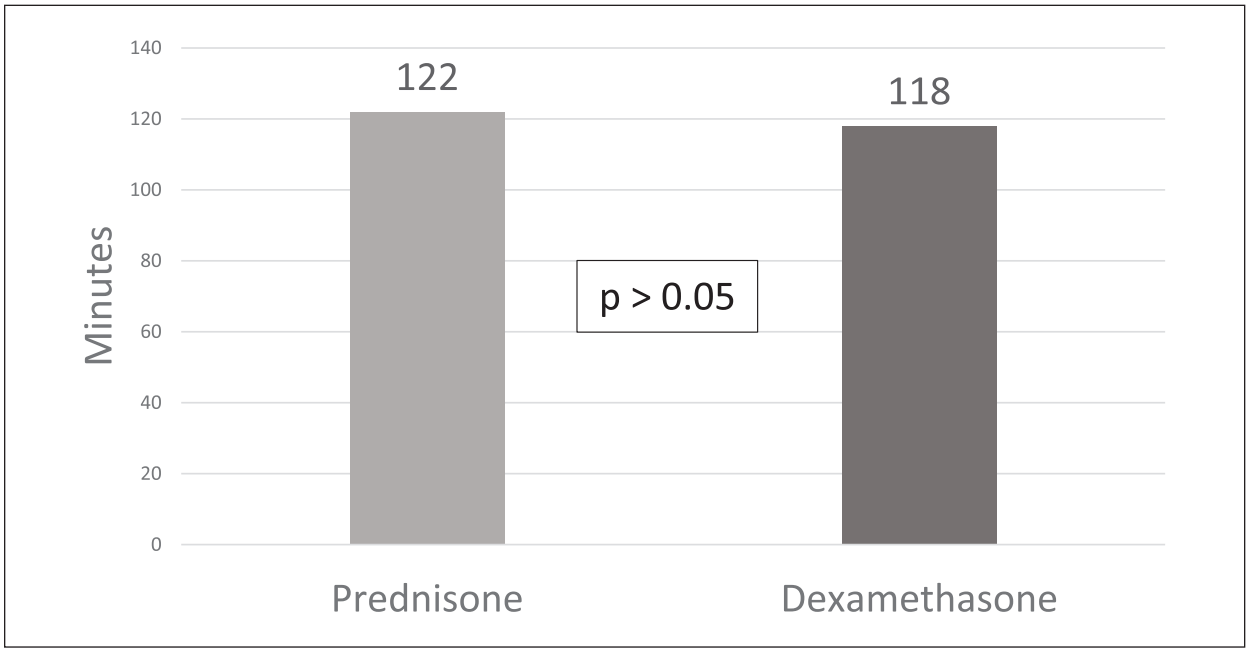

Figure 2. Average time to discharge from clinic.

relapse rate, return to baseline activity, and changes in asthma score, there was no difference between the 2 groups.[27] Parikh et al conducted a multicenter retrospective study, also revealing no difference in readmission rates or transfers to the intensive care unit when using either medication for hospitalized patients. They did show, however, a significant decrease in length of hospital stay and costs in the dexamethasone group.[14]

Oral dexamethasone has also been shown to be better tolerated than oral prednisone with regard to taste and decreased incidence of vomiting.[18,25,26] It is also more likely to have a higher adherence rate based on its shorter treatment duration of 2-days.[32] After administration of the first dose at the Center, only one additional dose is required at home, and the medication is dispensed from the Center's pharmacy prior to the patient leaving the clinic. Cooper et al have reported a low rate of only 45% of prescriptions, for prednisone and prednisolone were actually filled after discharge from the ED.[33]

Our study aimed to offer insight in lessening the burden of this chronic childhood disease. Asthma affects over 6 million children in the United States, and over 50% of these children have reported experiencing one or more asthma attacks.[1] With a high morbidity, asthma has contributed to over 136 000 pediatric hospital admissions in 2010,[1] and 13.8 million missed school days in 2013.[1] Children are more likely to use the ED as a primary health care facility if they have a diagnosis of asthma (3.4%) compared with children without asthma (2.1%),[1] with 17.2% of asthmatic children reporting an emergency room or urgent care visit in the past 12 months.[1] Currently, approximately 47.6% of children with asthma have Medicaid/CHIP as their primary insurance provider.[1,9]

This study further concluded that a 2-day course of dexamethasone prescribed in the primary care setting was not only clinically effective in the treatment of asthma symptoms but cost-effective as well. As mentioned earlier, patients picked up their second dose of dexamethasone at the Center's pharmacy prior to leaving the clinic. By providing the additional dose to patients, we can also infer increased compliance[33] and a decreased cost as seen in the study by Andrew et al, with a 50% cost reduction seen if the second dose of dexamethasone was dispended prior to leaving the ED.[21] We estimated the cost for a 2-day course of oral dexamethasone at US$1.28 and the cost for a 5-day course of prednisolone at US$16.20, generating a cost savings of US$14.92 per patient with the use of the dexamethasone therapy. Costs were calculated for a 23-kg male patient, which is the 50th percentile weight for a 7-year-old male.[31]

In addition to cost savings by using dexamethasone, we also reported a decreased cost for patients treated in the primary care setting as opposed to the ED. Using insurance claims, the average cost for an asthma exacerbation visit at the Center was found to be US$79.89. This is substantially lower than the cost in the ED, which averaged US$3113.28 per visit. We have demonstrated a significant reduction in direct costs, and based on data in the literature, we can also infer a decrease in indirect costs. A study by Andrews et al investigated the cost-effectiveness of the 2-day course of dexamethasone compared with the 5-day course of prednisone by also including the cost of missed work days of the parent or legal guardian.[21] They reported a cost savings of US$3500 per 100 patients treated in the ED when the additional dose of dexamethasone was prescribed. Interestingly, they reported a cost savings of US$7000 per 100 patients if the second dose of dexamethasone was dispensed prior to leaving the ED.[21] All costs can be lowered with early administration of corticosteroids for asthma exacerbations, which a study by Bhogal et al showed can reduce the odds of hospital admissions and length of treatment.[29] Therefore, it is important that primary care physicians become familiar with symptoms of an asthma exacerbation and begin early treatment with corticosteroids and β-agonists. One obstacle faced by primary care physicians in implementing the rapid administration of corticosteroids and β-agonists for patients with asthma exacerbation is time. In our study, the average clinic time for a patient was around 2 hours. However, in a patient-centered medical home where a team-based approach to care is utilized, face-to-face physician time can be decreased. Furthermore, appropriate documentation and coding can ensure compensation for the provider.

As mentioned above, providing treatment at the primary care level has proven effective in the treatment of asthma exacerbations and can help eliminate the burden placed on EDs and publicly funded insurances such as Medicaid and CHIP. ED overcrowding has been attributed to visits ultimately classified as nonemergent. This in turn leads to long wait times, increased patient morbidity, increased costs, and patient dissatisfaction.[34] Reducing nonemergent ED visits will allow improved management of true emergent situations. As asthma visits are a big contributor to ED overcrowding, our study reveals that acute exacerbations can safely and effectively be managed in the ambulatory setting. A main contributor of ED overcrowding for nonemergent situations has included lack of access to primary care services during nonstandard business hours.[35] A unique feature of the Center is its accessibility as a primary care center. The clinic is open 7 days a week with extended hours (7 AM until 11 PM on weekdays and 9 AM to 7 PM on weekend days). This allows increased access to the Center's services for patients who cannot arrive during standard business hours.[30]

Although our study demonstrates the clinical and cost-effectiveness in the use of oral dexamethasone in a primary care setting for acute asthma symptoms, limitations are present. The main limitation of the study is its retrospective nature. As the EMR was surveyed, errors may exist in coding and documentation. Being a retrospective study, specific questions and information could not be obtained from the patient or caregivers. We were unable to determine the true illness severity as measured by the number of previous exacerbations and the dose or duration of inhaled corticosteroids. Call backs were not done to determine medication compliance or medication adverse effects. Another limitation is that insurance claims from outside health facilities could not be tracked for 16% of patients, so we do not know if they were treated for wheezing elsewhere. However, if a patient was seen at a hospital in the Houston, Texas, area, which uses Epic EMR, the visit would be accessible through

chart review. We also do not know if patients had concurrent illnesses including pneumonia, which would have increased their severity of disease.

Conclusion

Asthma places a significant burden on patients, caregivers, health care systems, and financial institutions. Providing safe and effective care is the ultimate goal in treating pediatric asthma. This study has demonstrated that a 2-day course of oral dexamethasone appears to be a promising clinical and cost-effective alternative to 5 days of prednisone to manage acute asthma exacerbations at the primary care level. As a comprehensive primary care clinic, the Center has shown that the treatment of acute asthma exacerbations can effectively be treated in the ambulatory setting at a much lower cost than the ED.

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Author Contributions

NMN, SAM, and HLS contributed to the conception and design of the study. NMN, SAM, BSR, and LR contributed to the acquisition, analysis, and interpretation. NMN, ASV, SAM, and HLS drafted and crticically revised the manuscript. All authors gave final approval. NMN agrees to be accountable for all aspects of work ensuring integrity and accuracy.

Declaration of Conflicting Interests

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